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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,159	08/15/2001	Tania Kastelic	1556.0290000	9266

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EXAMINER

QIAN, CELINE X

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 11/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,159	KASTELIC ET AL.	
	Examiner	Art Unit	
	Celine X Qian	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-9 and 15-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-9 and 15-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 June 2001 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>7</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1, 3-9, 15-17 are pending in the application.

This Office Action is in response to the Amendment filed on 8/27/03.

Response to Amendment

The objection to claims 10 and 11 is moot in light of Applicant's cancellation of the claims.

The rejection of claim 11 under 35 U.S.C. 112 1st paragraph is moot in light of Applicant's cancellation of the claim.

The rejection of claims 4, 5, 8, 9, 16 and 17 under 35 U.S.C. 112 2nd paragraph has been withdrawn in light of Applicant's amendment of the claims.

The rejection of claims 4-7, 16 and 17 under 35 U.S.C. 102 (b) is maintained for reasons set forth of the record mailed on 6/17/03 and further discussed below.

The rejection of claims 1, 3 and 15 under 35 U.S.C. 103 (a) is maintained for reasons set forth of the record mailed on 6/17/03 and further discussed below.

Claims 8 and 9 are rejected under 35 U.S.C. 103 (a) for reasons discussed below.

Response to Arguments

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 4-7, 16 and 17 rejected under 35 U.S.C. 102(b) as being anticipated by Banholzer et al.

In response to this rejection, Applicant argues that the amended claims include the limitation that an instability region consisting of at least 20-100 nucleotides of the 3' UTR of a gene sequence which confers instability to a mRNA, wherein the instability region is inserted into the 3' UTR of the expression cassette, and such limitation is not disclosed by Banholzer et al. Particularly, Applicant argues that Banholzer does not disclose the insertion of a heterologous 3' UTR into the 3' UTR of a reporter gene.

This argument has been fully considered but deemed unpersuasive. The disclosure of Banholzer was discussed in detail in the office action mailed on 6/17/03. Briefly, Banholzer discloses an expression construct comprising a gene encoding a protein, 5' and 3' UTR sequences comprising control elements and instability sequences, wherein the 3' UTR comprising the instability sequence is inserted into the construct. Contrary to Applicant's assertion, the above mentioned claim limitation does not differentiate whether the inserted 3' UTR is heterologous to the 3' UTR of gene encoding a protein having a detectable signal. Consequently, the claimed construct has the same elements as the construct disclosed by Banholzer. Therefore, the disclosure of Banholzer anticipates the claimed invention, and the rejection is maintained.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banholzer et al., in view of Zhang et al (1996, BBRC, vol.227, pages 707-711).

The reasons for the obviousness rejection were discussed in detail in the office action mailed on 6/17/03. In response to this rejection, Applicant argues that the deficiency of Banholzer et al., namely, using of a reporter gene for screening compounds that affect mRNA stability, is not cured by the disclosure of Zhang et al. Applicant asserts that Zhang does not disclose, suggest, or contemplate a method of screening compounds that affect the stability of mRNA using a reporter gene DNA expression system as disclosed by the instant application. Applicant further asserts that the skilled artisan would not have found motivation to combine the references because Banholzer does not disclose, suggest, or contemplate the use of a reporter gene construct as disclosed in Zhang, and Zhang does not disclose or suggest the use of GFP reporter gene for use in screening for compounds that induce mRNA instability. Applicant thus concludes that the invention is not obvious in view of the cited references.

The above arguments have been fully considered but deemed unpersuasive. The teachings of Banholzer and Zhang were discussed in detail in the office action mailed on 6/27/03. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071,

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5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation of combining the references comes from the teaching that GFP is an important reporter because it has advantages over other reporter for not requiring additional cofactors, substrates, or additional gene products as taught by Zhang. Zhang does not limit the use of GFP to any particular reporter gene system. One of ordinary skill of art would readily recognize that the system for screening compounds that affect mRNA instability taught by Banholzer can take advantage of using GFP as a reporter gene for easy detection. Therefore, the combined teachings of Banholzer and Zhang render the claimed invention obvious.

New Grounds of Rejection Necessitated by Applicant's Amendment

Claims 8 and 9 rejected under 35 U.S.C. 103(a) as being unpatentable over Danner et al., 1998 (AS4), Banhozler et al., in view of Maniatis et al. (1987).

The teachings of Danner, Banholzer and Maniatis were discussed in detail in the office action mailed on 6/17/03. The reasons for this obviousness rejection were also discussed in the previous office action (see pages 8 and 9).

In response to this rejection, Applicant argues that the amended claims include the limitation of an instability consisting of at least 20-100 nucleotides of the 3' UTR of a gene sequence which confers instability to a mRNA, wherein the instability region is inserted into 3' UTR of the expression cassette, such limitation is not taught by Danner et al. Applicant further asserts that Danner does not disclose, suggest or contemplate a method of screening for compounds that affect the stability of mRNA, or assays designed to achieve this. Applicant

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asserts that such deficiency is not cured by Manniatis, and thus concludes that the invention is not obvious in view of the cited references.

The above arguments have been fully considered but deemed unpersuasive. Although Danner does not teach the insertion of an mRNA instability region into 3' UTR of the expression cassette, Danner teaches a cell line transfected with a wild type β 2AR expression vector, a β -globulin expression vector and a chimeric expression vector comprising β -globulin and 3'UTR of β 2AR (either with or without mRNA instability sequence). The chimeric expression vector comprises all the elements of the claimed expression construct. In addition, the mRNA instability sequence has been identified. As such, whether the presence of the mRNA instability sequence in the expression vector is result from insertion or other methods does not affect the functional characteristic of the instability of the sequence, and the ability of the expression vector for identifying compounds that affect such instability sequence. Although Danner does not teach a method of screening for compounds that affect the stability of mRNA, Danner teaches that compounds such as forskolin and isoproterenol affect the mRNA stability in the testing system comprising cells co-transfected with a wild type β 2AR expression vector, a β -globulin expression vector and a chimeric expression vector comprising β -globulin and 3'UTR of β 2AR (see page 3227, 2nd paragraph). It would have been obvious to one of ordinary skill or art to use such system or assay to screening compounds that affect mRNA instability because of such teaching. In addition, Banholzer teaches a method and assay system that identifies rapamycin and FK506 as compounds that induce mRNA degradation. The difference between the claimed invention and the assay system taught by Banholzer is the claimed invention co-transfected all expression cassette into one cell line. Since co-transfection of such system is taught by Danner,

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it would have been obvious to one of ordinary skill of art to use cell line co-transfected with constructs taught by either Danner or Banholzer et al. to screen compounds that affect mRNA stability. Manniatis teach method of stable transfection. In view of the combined teaching of the above references, the invention would have been obvious to one of ordinary skill of art at the time the invention was made.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.

Anne-Marie Falk
ANNE-MARIE FALK, PH.D.
PRIMARY EXAMINER